

FIG. 1.

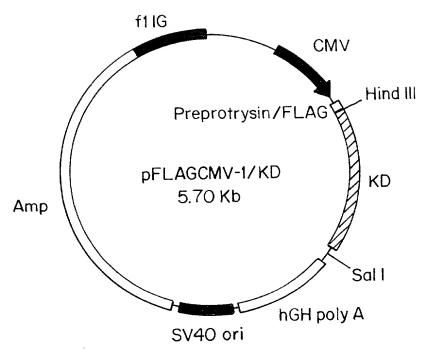


FIG. 2.

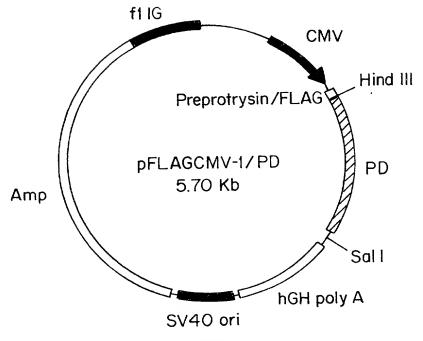
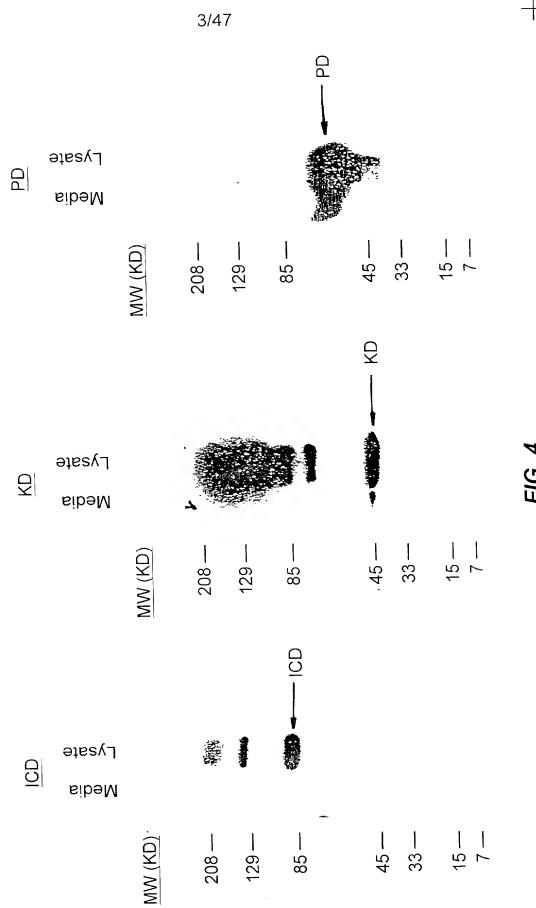


FIG. 3.



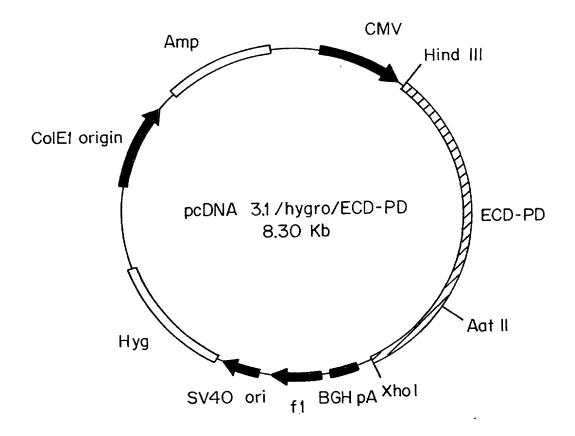
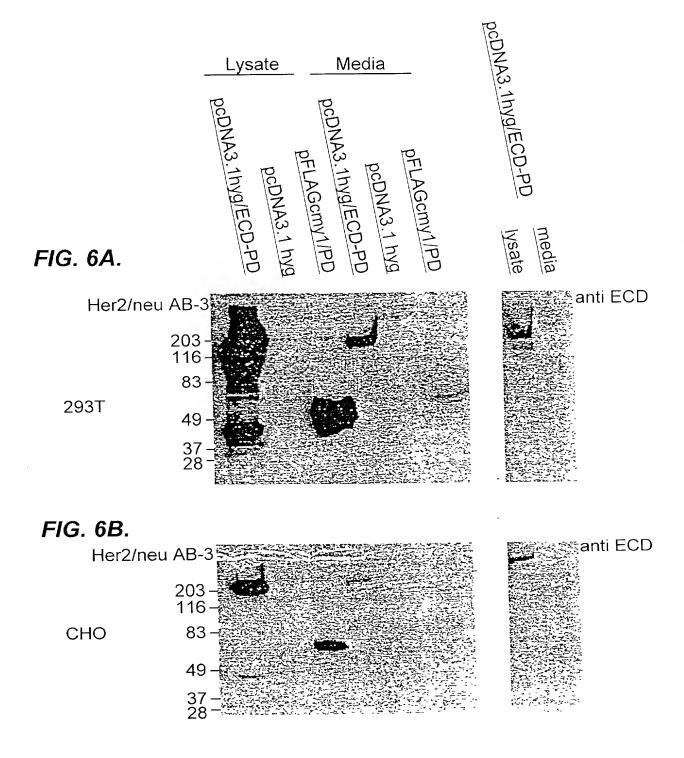


FIG. 5.

pcDNA3.1hyg/ECD-PD expression



Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu

FIG. 7. (SEQ ID NO: 1)

His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His

FIG. 7. (CONTINUED)

Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser Ile Ile Ser Ala Val Val Gly Ile Leu Leu Val Val Leu Gly Val Val Phe Gly Ile Leu Ile Lys Arg Arg Gln Gln Lys Ile Arg Lys Tyr Thr Met Arg Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser Gly Ala Met Pro Asn Gln Ala Gln Met Arg Ile Leu Lys Glu Thr Glu Leu Arg Lys Val Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr Lys Gly Ile Trp Ile Pro Asp Gly Glu Asn Val Lys Ile Pro Val Ala Ile Lys Val Leu Arg Glu Asn Thr Ser Pro Lys Ala Asn Lys Glu Ile Leu

FIG. 7. (CONTINUED)

Asp Glu Ala Tyr Val Met Ala Gly Val Gly Ser Pro Tyr Val Ser Arg Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Val Thr Gln Leu Met Pro Tyr Gly Cys Leu Leu Asp His Val Arg Glu Asn Arg Gly Arg Leu Gly Ser Gln Asp Leu Leu Asn Trp Cys Met Gln Ile Ala Lys Gly Met Ser Tyr Leu Glu Asp Val Arg Leu Val His Arg Asp Leu Ala Ala Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys Ile Thr Asp Phe Gly Leu Ala Arg Leu Leu Asp Ile Asp Glu Thr Glu Tyr His Ala Asp Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu Arg Arg Arg Phe Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr Val Trp Glu Leu Met Thr Phe Gly Ala Lys Pro Tyr Asp Gly Ile Pro Ala Arg Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln Pro Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp Met Ile Asp Ser Glu Cys Arg Pro Arg Phe Arg Glu Leu Val Ser Glu Phe Ser Arg Met Ala Arg Asp Pro Gln Arg Phe Val Val Ile Gln Asn Glu Asp Leu Gly Pro Ala Ser Pro Leu Asp Ser Thr Phe Tyr Arg Ser Leu Leu Glu Asp Asp Met Gly Asp Leu Val Asp Ala Glu Glu Tyr Leu

Val 1025		Gln	Gln	_	Phe .030	Phe	Cys	Pro		Pro .035	Ala	Pro	Gly		Gly .040
Gly	Met	Val		His .045	Arg	His	Arg		Ser L050	Ser	Thr	Arg		Gly .055	Gly
Gly	Asp		Thr 1060	Leu	Gly	Leu		Pro .065	Ser	Glu	Glu	Glu 1	Ala 1070	Pro	Arg
Ser		Leu 1075	Ala	Pro	Ser		Gly L080	Ala	Gly	Ser		Val 1085	Phe	Asp	Gly
	Leu L090	Gly	Met	Gly		Ala 1095	Lys	Gly	Leu		Ser L100	Leu	Pro	Thr	His
Asp 1105		Ser	Pro		Gln 1110	Arg	Tyr	Ser		Asp 1115	Pro	Thr	Val		Leu 120
Pro	Ser	Glu		Asp L125	Gly	Tyr	Val		Pro 1130	Leu	Thr	Cys		Pro 1135	Gln
Pro	Glu	_	Val 1140	Asn	Gln	Pro	_	Val 1145	Arg	Pro	Gln	Pro	Pro 1150	Ser	Pro
Arg		Gly 1155	Pro	Leu	Pro		Ala 1160	Arg	Pro	Ala	_	Ala 1165	Thr	Leu	Glu
_	Pro 1170	Lys	Thr	Leu		Pro 1175	Gly	Lys	Asn		Val 1180	Val	Lys	Asp	Val
Phe 118		Phe	Gly	_	Ala 1190	Val	Glu	Asn		Glu 1195	Tyr	Leu	Thr		Gln 1200
Gly	Gly	Ala		Pro 1205	Gln	Pro	His		Pro 1210	Pro	Ala	Phe		Pro 1215	Ala
Phe	Asp		Leu 1220	Tyr	Tyr	Trp		Gln 1225	Asp	Pro	Pro	Glu	Arg 1230	Gly	Ala
Pro		Ser 1235	Thr	Phe	Lys		Thr 1240	Pro	Thr	Ala		Asn 1245	Pro	Glu	Tyr
	Gly 1250	Leu	Asp	Val		Val 1255	*	* 12	57						

FIG. 7. (CONTINUED)

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Met Glu Leu Ala Ala Trp Cys Arg Trp Gly Phe Leu Leu Ala Leu Leu Pro Pro Gly Ile Ala Gly Thr Gln Val Cys Thr Gly Thr Asp Met Lys Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr Val Pro Ala Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val Gln Gly Tyr Met Leu Ile Ala His Asn Gln Val Lys Arg Val Pro Leu Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Lys Tyr Ala Leu Ala Val Leu Asp Asn Arg Asp Pro Gln Asp Asn Val Ala Ala Ser Thr Pro Gly Arg Thr Pro Glu Gly Leu Arg Glu Leu Gln Leu Arg Ser Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Arg Gly Asn Pro Gln Leu Cys Tyr Gln Asp Met Val Leu Trp Lys Asp Val Phe Arg Lys Asn Asn Gln Leu Ala Pro Val Asp Ile Asp Thr Asn Arg Ser Arg Ala Cys Pro Pro Cys Ala Pro Ala Cys Lys Asp Asn His Cys Trp Gly Glu Ser Pro Glu Asp Cys Gln Ile Leu Thr Gly Thr Ile Cys Thr Ser Gly Cys Ala Arg Cys Lys Gly Arg Leu Pro Thr Asp Cys Cys His Glu Gln Cys Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys

FIG. 8. (SEQ ID NO:2)

Leu His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met His Asn Pro Glu Gly Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Thr Cys Pro Tyr Asn Tyr Leu Ser Thr Glu Val Gly Ser Cys Thr Leu Val Cys Pro Pro Asn Asn Gln Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Gly Ala Arg Ala Ile Thr Ser Asp Asn Val Gln Glu Phe Asp Gly Cys Lys Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp Pro Ser Ser Gly Ile Ala Pro Leu Arg Pro Glu Gln Leu Gln Val Phe Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu Arg Asp Leu Ser Val Phe Gln Asn Leu Arg Ile Ile Arg Gly Arg Ile Leu His Asp Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu Gly Ile His Ser Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu Ala Leu Ile His Arg Asn Ala His Leu Cys Phe Val His Thr Val Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Ser Gly Asn Arg Pro Glu Glu Asp Cys Gly Leu Glu Gly Leu Val Cys

Asn Ser Leu Cys Ala His Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys Val Asn Cys Ser His Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys Arg Val Trp Lys Gly Leu Pro Arg Glu Tyr Val Ser Asp Lys Arg Cys Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Ser Ser Glu Thr Cys Phe Gly Ser Glu Ala Asp Gln Cys Ala Ala Cys Ala His Tyr Lys Asp Ser Ser Ser Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu Ser Tyr Met Pro Ile Trp Lys Tyr Pro Asp Glu Glu Gly Ile Cys Gln Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Glu Arg Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Val Thr Phe Ile Ile Ala Thr Val Glu Gly Val Leu Leu Phe Leu Ile Leu Val Val Val Gly Ile Leu Ile Lys Arg Arg Gln Lys Ile Arg Lys Tyr Thr Met Arg Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser Gly Ala Met Pro Asn Gln Ala Gln Met Arg Ile Leu Lys Glu Thr Glu Leu Arg Lys Val Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr Lys Gly Ile Trp Ile Pro Asp Gly Glu Asn Val Lys Ile Pro Val Ala Ile Lys Val Leu Arg Glu Asn Thr Ser Pro Lys Ala Asn Lys Glu Ile

Leu Asp Glu Ala Tyr Val Met Ala Gly Val Gly Ser Pro Tyr Val Ser Arg Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Val Thr Gln Leu Met Pro Tyr Gly Cys Leu Leu Asp His Val Arg Glu His Arg Gly Arg Leu Gly Ser Gln Asp Leu Leu Asn Trp Cys Val Gln Ile Ala Lys Gly Met Ser Tyr Leu Glu Asp Val Arg Leu Val His Arg Asp Leu Ala Ala Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys Ile Thr Asp Phe Gly Leu Ala Arg Leu Leu Asp Ile Asp Glu Thr Glu Tyr His Ala Asp Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu Arg Arg Arg Phe Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr Val Trp Glu Leu Met Thr Phe Gly Ala Lys Pro Tyr Asp Gly Ile Pro Ala Arg Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln Pro Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp Met Ile Asp Ser Glu Cys Arg Pro Arg Phe Arg Glu Leu Val Ser Glu Phe Ser Arg Met Ala Arg Asp Pro Gln Arg Phe Val Val Ile Gln Asn Glu Asp Leu Gly Pro Ser Ser Pro Met Asp Ser Thr Phe Tyr Arg Ser Leu Leu Glu Asp Asp Met Gly Asp Leu Val Asp Ala Glu Glu Tyr

Leu ' 1025	Val	Pro	Gln	Gln (Gly 030	Phe	Phe	Ser	Pro A	Asp 035	Pro '	Thr	Pro (Gly 1	Chr 040
Gly	Ser	Thr		His .	Arg	Arg	His	Arg 1	Ser :	Ser	Ser	Thr	Arg 1	Ser (055	Gly
Gly	Gly		Leu 1060	Thr	Leu	Gly	Leu 1	Glu 065	Pro	Ser	Glu	Glu 1	Gly 070	Pro :	Pro
Arg		Pro .075	Leu	Ala	Pro		Glu .080	Gly	Ala	Gly	Ser 1	Asp .085	Val	Phe 1	Asp
	Asp .090	Leu	Ala	Met	Gly 1	Val .095	Thr	Lys	Gly	Leu 1	Gln .100	Ser	Leu	Ser	Pro
His 1105		Leu	Ser	Pro 1	Leu 110	Gln	Arg	Tyr	Ser	Glu 115	Asp	Pro	Thr	Leu 1	Pro 120
Leu	Pro	Pro		Thr 1125	Asp	Gly	Tyr	Val	Ala 1130	Pro	Leu	Ala	Cys 1	Ser 135	Pro
Gln	Pro		Tyr 1140	Val	Asn	Gln	Ser	Glu 1145	Val	Gln	Pro	Gln	Pro 1150	Pro	Leu
Thr		Glu 1155		Pro	Leu		Pro 1160	Val	Arg	Pro	Ala	Gly 1165	Ala	Thr	Leu
	Arg 1170	Pro	Lys	Thr	Leu	Ser 1175	Pro	Gly	Lys	Asn	Gly 1180	Val	Val	Lys	Asp
Val 118		Ala	Ph∈	e Gly	Gly 1190	Ala	Val	Glu	Asn	Pro 1195	Glu	Tyr	Leu	Val	Pro 1200
Arg	Glu	Gly	7 Thr	Ala 1205		Pro	Pro	His	Pro 1210	Ser	Pro	Ala	Phe	Ser 1215	Pro
Ala	Phe	. Asp	Asr 1220	n Leu)	Tyr	Tyr	Trp	Asp 1225	Gln	Asn	Ser	Ser	Glu 1230	Gln	Gly
Pro	Pro	Pro 1235		r Asn	. Phe	e Glu	1 Gly		Pro	Thr	Ala	Glu 1245	Asn	Pro	Glu
Tyr	Leu 1250		y Le	u Asp	val	Pro 1255		*	* 125	8					

Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Ala Leu Leu Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu

FIG. 9. (SEQ ID NO: 3)

His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His

Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys 525 515 520 Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys 535 530 Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys 550 Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys 565 570 Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp 585 Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu 595 605 Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln 620 610 615 Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys 640 630 625 Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser

FIG. 9. (CONTINUED)

645

650

Gln Asn Glu Asp Leu Gly Pro Ala Ser Pro Leu Asp Ser Thr Phe Tyr 15

Arg Ser Leu Leu Glu Asp Asp Asp Met Gly Asp Leu Val Asp Ala Glu 30

Glu Tyr Leu Val Pro Gln Gln Gly Phe Phe Cys Pro Asp Pro Ala Pro 45

Gly Ala Gly Gly Met Val His His Arg His Arg Ser Ser Ser Thr Arg 60

Ser Gly Gly Gly Asp Leu Thr Leu Gly Leu Glu Pro Ser Glu Glu Glu 65

Ala Pro Arg Ser Pro Leu Ala Pro Ser Glu Gly Ala Gly Ser Asp Val 95

FIG. 10. (SEQ ID NO: 4)

Phe Asp Gly Asp Leu Gly Met Gly Ala Ala Lys Gly Leu Gln Ser Leu Pro Thr His Asp Pro Ser Pro Leu Gln Arg Tyr Ser Glu Asp Pro Thr Val Pro Leu Pro Ser Glu Thr Asp Gly Tyr Val Ala Pro Leu Thr Cys Ser Pro Gln Pro Glu Tyr Val Asn Gln Pro Asp Val Arg Pro Gln Pro Pro Ser Pro Arg Glu Gly Pro Leu Pro Ala Ala Arg Pro Ala Gly Ala Thr Leu Glu Arg Pro Lys Thr Leu Ser Pro Gly Lys Asn Gly Val Val Lys Asp Val Phe Ala Phe Gly Gly Ala Val Glu Asn Pro Glu Tyr Leu Thr Pro Gln Gly Gly Ala Ala Pro Gln Pro His Pro Pro Pro Ala Phe Ser Pro Ala Phe Asp Asn Leu Tyr Tyr Trp Asp Gln Asp Pro Pro Glu Arg Gly Ala Pro Pro Ser Thr Phe Lys Gly Thr Pro Thr Ala Glu Asn Pro Glu Tyr Leu Gly Leu Asp Val Pro Val

FIG. 10. (CONTINUED)

FIG. 11. (SEQ ID NO: 5)

Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Ala Leu Leu Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu

FIG. 12. (SEQ ID NO: 6)

His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu Val Arq Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His

Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser Gln Asn Glu Asp Leu Gly Pro Ala Ser Pro Leu Asp Ser Thr Phe Tyr Arg Ser Leu Leu Glu Asp Asp Met Gly Asp Leu Val Asp Ala Glu Glu Tyr Leu Val Pro Gln Gly Phe Phe Cys Pro Asp Pro Ala Pro Gly Ala Gly Gly Met Val His His Arg His Arg Ser Ser Ser Thr Arg Ser Gly Gly Gly Asp Leu Thr Leu Gly Leu Glu Pro Ser Glu Glu Glu Ala Pro Arg Ser Pro Leu Ala Pro Ser Glu Gly Ala Gly Ser Asp Val Phe Asp Gly Asp Leu Gly Met Gly Ala Ala Lys Gly Leu Gln Ser Leu Pro Thr His

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Asp	Pro 770	Ser	Pro	Leu	Gln	Arg 775	Tyr	Ser	Glu	Asp	Pro 780	Thr	Val	Pro	Leu
Pro 785	Ser	Glu	Thr	Asp	Gly 790	Tyr	Val	Ala	Pro	Leu 795	Thr	Cys	Ser	Pro	Gln 800
Pro	Glu	Tyr	Val	Asn 805	Gln	Pro	Asp	Val	Arg 810	Pro	Gln	Pro	Pro	Ser 815	Pro
Arg	Glu	Gly	Pro 820	Leu	Pro	Ala	Ala	Arg 825	Pro	Ala	Gly	Ala	Thr 830	Leu	Glu
Arg	Pro	Lys 835	Thr	Leu	Ser	Pro	Gly 840	Lys	Asn	Gly	Val	Val 845	Lys	Asp	Val
Phe	Ala 850	Phe	Gly	Gly	Ala	Val 855	Glu	Asn	Pro	Glu	Tyr 860	Leu	Thr	Pro	Gln
Gly 865	Gly	Ala	Ala	Pro	Gln 870	Pro	His	Pro	Pro	Pro 875	Ala	Phe	Ser	Pro	Ala 880
Phe	Asp	Asn	Leu	Tyr 885	Tyr	Trp	Asp	Gln	Asp 890	Pro	Pro	Glu	Arg	Gly 895	Ala
Pro	Pro	Ser	Thr 900	Phe	Lys	Gly	Thr	Pro 905	Thr	Ala	Glu	Asn	Pro 910	Glu	Tyr
Leu	_	Leu 915	Asp	Val	Pro	Val 920	*								

FIG. 12. (CONTINUED)

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Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Ala Leu Leu Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu

FIG. 13. (SEQ ID NO: 7)

His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His

							20	0/4/							
Gln	Leu	Cys 515	Ala	Arg	Gly	His	Cys 520	Trp	Gly	Pro	Gly	Pro 525	Thr	Gln	Cys
Val	Asn 530	Cys	Ser	Gln	Phe	Leu 535	Arg	Gly	Gln	Glu	Cys 540	Val	Glu	Glu	Cys
Arg 545	Val	Leu	Gln	Gly	Leu 550	Pro	Arg	Glu	Tyr	Val 555	Asn	Ala	Arg	His	Cys 560
Leu	Pro	Cys	His	Pro 565	Glu	Cys	Gln	Pro	Gln 570	Asn	Gly	Ser	Val	Thr 575	Cys
Phe	Gly	Pro	Glu 580	Ala	Asp	Gln	Cys	Val 585	Ala	Cys	Ala	His	Tyr 590	Lys	Asp
Pro	Pro	Phe 595	Cys	Val	Ala	Arg	Cys 600	Pro	Ser	Gly	Val	Lys 605	Pro	Asp	Leu
Ser	Tyr 610	Met	Pro	Ile	Trp	Lys 615	Phe	Pro	Asp	Glu	Glu 620	Gly	Ala	Cys	Gln
Pro 625	Cys	Pro	Ile	Asn	Cys 630	Thr	His	Ser	Cys	Val 635	Asp	Leu	Asp	Asp	Lys 640
Gly	Cys	Pro	Ala	Glu 645	Gln	Arg	Ala	Ser	Pro 650	Leu	Thr	Ser	Gln	Asn 655	Glu
Asp	Leu	Gly	Pro 660	Ala	Ser	Pro	Leu	Asp 665	Ser	Thr	Phe	Tyr	Arg 670	Ser	Leu
Leu	Glu	Asp 675	Asp	Asp	Met	Gly	Asp 680	Leu	Val	Asp	Ala	Glu .685	Glu	Tyr	Leu
Val	Pro 690	Gln	Gln	Gly	Phe	Phe 695	Cys	Pro	Asp	Pro	Ala 700	Pro	Gly	Ala	Gly
Gly 705	Met	Val	His	His	Arg 710	His	Arg	*	* 714						

FIG. 13.(CONTINUED)

Met Glu Leu Ala Ala Trp Cys Arg Trp Gly Phe Leu Leu Ala Leu Leu Pro Pro Gly Ile Ala Gly Thr Gln Val Cys Thr Gly Thr Asp Met Lys Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr Val Pro Ala Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val Gln Gly Tyr Met Leu Ile Ala His Asn Gln Val Lys Arg Val Pro Leu Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Lys Tyr Ala Leu Ala Val Leu Asp Asn Arg Asp Pro Gln Asp Asn Val Ala Ala Ser Thr Pro Gly Arg Thr Pro Glu Gly Leu Arg Glu Leu Gln Leu Arg Ser Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Arg Gly Asn Pro Gln Leu Cys Tyr Gln Asp Met Val Leu Trp Lys Asp Val Phe Arg Lys Asn Asn Gln Leu Ala Pro Val Asp Ile Asp Thr Asn Arg Ser Arg Ala Cys Pro Pro Cys Ala Pro Ala Cys Lys Asp Asn His Cys Trp Gly Glu Ser Pro Glu Asp Cys Gln Ile Leu Thr Gly Thr Ile Cys Thr Ser Gly Cys Ala Arg Cys Lys Gly Arg Leu Pro Thr Asp Cys Cys His Glu Gln Cys Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys

FIG. 14. (SEQ ID NO: 8)

Leu His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met His Asn Pro Glu Gly Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Thr Cys Pro Tyr Asn Tyr Leu Ser Thr Glu Val Gly Ser Cys Thr Leu Val Cys Pro Pro Asn Asn Gln Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Gly Ala Arq Ala Ile Thr Ser Asp Asn Val Gln Glu Phe Asp Gly Cys Lys Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp Pro Ser Ser Gly Ile Ala Pro Leu Arg Pro Glu Gln Leu Gln Val Phe Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu Arg Asp Leu Ser Val Phe Gln Asn Leu Arg Ile Ile Arg Gly Arg Ile Leu His Asp Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu Gly Ile His Ser Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu Ala Leu Ile His Arg Asn Ala His Leu Cys Phe Val His Thr Val Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Ser Gly Asn Arg Pro Glu Glu Asp Cys Gly Leu Glu Gly Leu Val Cys

FIG. 14. (CONTINUED)

Asn Ser Leu Cys Ala His Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys Val Asn Cys Ser His Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys Arg Val Trp Lys Gly Leu Pro Arg Glu Tyr Val Ser Asp Lys Arg Cys Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Ser Ser Glu Thr Cys Phe Gly Ser Glu Ala Asp Gln Cys Ala Ala Cys Ala His Tyr Lys Asp Ser Ser Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu Ser Tyr Met Pro Ile Trp Lys Tyr Pro Asp Glu Glu Gly Ile Cys Gln Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Glu Arg Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Val Thr Phe

30/47															
					TTG Leu										45
					GCG Ala										90
					CCT Pro										135
					CAG Gln										180
					CCC Pro										225
					CAG Gln										270
					CTG Leu										315
CAG Gln	CTC Leu	TTT Phe	GAG Glu	GAC Asp 110	AAC Asn	TAT Tyr	GCC Ala	CTG Leu	GCC Ala 115	Val	CTA Leu	GAC Asp	AAT Asn	GGA Gly 120	360
GAC Asp	CCG Pro	CTG Leu	AAC Asn	AAT Asn 125	ACC Thr	ACC Thr	CCT Pro	GTC Val	ACA Thr 130	Gly	GCC Ala	TCC Ser	CCA Pro	GGA Gly 135	405
GGC Gly	CTG Leu	G CGG L Arg	GAG Glu	CTG Leu 140	CAG Gln	CTT Leu	CGA Arg	AGC Ser	CTC Leu 145	Thr	GAG Glu	ATC Ile	TTG Leu	AAA Lys 150	450
GGA Gly	GGG Gly	GTC Val	TTG Lev	ATC Ile 155	CAG Gln	CGG Arg	AAC Asn	CCC Pro	CAG Glr 160	l Leu	TGC Cys	TAC Tyr	CAG Gln	GAC Asp 165	495
ACC Thr	ATI	TTC e Lei	G TGC 1 Trp	F AAG Lys 170	G GAC S Asp	ATC Ile	TTC Phe	CAC His	AAC Lys	s Asr	C AAC n Asr	C CAG	G CTG	GCT Ala 180	540

FIG. 15. (SEQ ID NO:9)

								/47							i
					ACC Thr										585
					GGC Gly										630
					ACG Thr										675
					CTG Leu										720
					GGC Gly										765
					AGT Ser										810
					ACA Thr										855
GAG Glu	GGC Glu	CGG Arg	TAT Tyr	ACA Thr 290	TTC Phe	GGC Gly	GCC Ala	AGC Ser	TGT Cys 295	Val	ACT Thr	GCC Ala	TGT Cys	CCC Pro 300	900
TAC Tyr	AAC Asn	TAC Tyr	CTT Leu	TCT Ser 305	ACG Thr	GAC Asp	GTG Val	GGA Gly	TCC Ser 310	Cys	ACC Thr	CTC Leu	GTC Val	TGC Cys 315	945
					GAG Glu					Asp					990
					Lys					y Val					1035
					ı Arg					a Val				AAT Asn 360	1080

FIG. 15. (CONTINUED)

ATC CAG GAG TTT GCT GGC TGC AAG AAG ATC TTT GGG AGC CTG GCA 1125 Ile Gln Glu Phe Ala Gly Cys Lys Ile Phe Gly Ser Leu Ala 370 365 TTT CTG CCG GAG AGC TTT GAT GGG GAC CCA GCC TCC AAC ACT GCC 1170 Phe Leu Pro Glu Ser Phe Asp Gly Asp Pro Ala Ser Asn Thr Ala 385 390 380 CCG CTC CAG CCA GAG CAG CTC CAA GTG TTT GAG ACT CTG GAA GAG 1215 Pro Leu Gln Pro Glu Gln Leu Gln Val Phe Glu Thr Leu Glu Glu 400 ATC ACA GGT TAC CTA TAC ATC TCA GCA TGG CCG GAC AGC CTG CCT 1260 Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Asp Ser Leu Pro 415 420 410 GAC CTC AGC GTC TTC CAG AAC CTG CAA GTA ATC CGG GGA CGA ATT 1305 Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg Gly Arg Ile 430 435 425 CTG CAC AAT GGC GCC TAC TCG CTG ACC CTG CAA GGG CTG GGC ATC 1350 Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu Gly Ile 440 AGC TGG CTG GGG CTG CGC TCA CTG AGG GAA CTG GGC AGT GGA CTG 1395 Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu 465 460 455 GCC CTC ATC CAC CAT AAC ACC CAC CTC TGC TTC GTG CAC ACG GTG 1440 Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val 475 480 470 CCC TGG GAC CAG CTC TTT CGG AAC CCG CAC CAA GCT CTG CTC CAC 1485 Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His 495 485 ACT GCC AAC CGG CCA GAG GAC GAG TGT GTG GGC GAG GGC CTG GCC 1530 Thr Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala 505 510 500 TGC CAC CAG CTG TGC GCC CGA GGG CAC TGC TGG GGT CCA GGG CCC 1575 Cys His Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro 525 520 515 ACC CAG TGT GTC AAC TGC AGC CAG TTC CTT CGG GGC CAG GAG TGC 1620 Thr Gln Cys Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys 540 530

GTG GAG GAA TGC CGA GTA CTG CAG GGG CTC CCC AGG GAG TAT GTG 1665 Val Glu Glu Cys Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val 545 550 AAT GCC AGG CAC TGT TTG CCG TGC CAC CCT GAG TGT CAG CCC CAG 1710 Asn Ala Arg His Cys Leu Pro Cys His Pro Glu Cys Gln Pro Gln 560 565 570 AAT GGC TCA GTG ACC TGT TTT GGA CCG GAG GCT GAC CAG TGT GTG 1755 Asn Gly Ser Val Thr Cys Phe Gly Pro Glu Ala Asp Gln Cys Val 580 GCC TGT GCC CAC TAT AAG GAC CCT CCC TTC TGC GTG GCC CGC TGC 1800 Ala Cys Ala His Tyr Lys Asp Pro Pro Phe Cys Val Ala Arg Cys 595 590 CCC AGC GGT GTG AAA CCT GAC CTC TCC TAC ATG CCC ATC TGG AAG 1845 Pro Ser Gly Val Lys Pro Asp Leu Ser Tyr Met Pro Ile Trp Lys 610 605 TTT CCA GAT GAG GGC GCA TGC CAG CCT TGC CCC ATC AAC TGC 1890 Phe Pro Asp Glu Glu Gly Ala Cys Gln Pro Cys Pro Ile Asn Cys 620 625 ACC CAC TCC TGT GTG GAC CTG GAT GAC AAG GGC TGC CCC GCC GAG 1935 Thr His Ser Cys Val Asp Leu Asp Asp Lys Gly Cys Pro Ala Glu 645 640 635 CAG AGA GCC AGC CCT CTG ACG TCC ATC ATC TCT GCG GTG GTT GGC 1980 Gln Arg Ala Ser Pro Leu Thr Ser Ile Ile Ser Ala Val Gly 655 660 650 ATT CTG CTG GTC GTG GTC TTG GGG GTG GTC TTT GGG ATC CTC ATC 2025 Ile Leu Leu Val Val Val Leu Gly Val Val Phe Gly Ile Leu Ile 675 665 AAG CGA CGG CAG CAG AAG ATC CGG AAG TAC ACG ATG CGG AGA CTG 2070 Lys Arg Arg Gln Gln Lys Ile Arg Lys Tyr Thr Met Arg Arg Leu 685 690 680 CTG CAG GAA ACG GAG CTG GTG GAG CCG CTG ACA CCT AGC GGA GCG 2115 Leu Gln Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser Gly Ala 705 695 700 ATG CCC AAC CAG GCG CAG ATG CGG ATC CTG AAA GAG ACG GAG CTG 2160 Met Pro Asn Gln Ala Gln Met Arg Ile Leu Lys Glu Thr Glu Leu 710

FIG. 15. (CONTINUED)

							-	141							
			AAG Lys												2205
			TGG Trp												2250
			GTG Val												2295
GAA Glu	ATC Ile	TTA Leu	GAC Asp	GAA Glu 770	GCA Ala	TAC Tyr	GTG Val	ATG Met	GCT Ala 775	GGT Gly	GTG Val	GGC Gly	TCC Ser	CCA Pro 780	2340
			CGC Arg												2385
			CAG Gln												2430
CGG Arg	GAA Glu	AAC Asn	CGC Arg	GGA Gly 815	CGC Arg	CTG Leu	GGC Gly	TCC Ser	CAG Gln 820	GAC Asp	CTG Leu	CTG Leu	AAC Asn	TGG Trp 825	2475
			ATT												2520
		His	AGG Arg	Asp	Leu	Ala	Ala	Arg	Asn	Val	Leu		Lys		2565
CCC Pro	AAC Asn	CAT His	GTC Val	AAA Lys 860	Ile	ACA Thr	GAC Asp	TTC Phe	GGG Gly 865	Let	GCT Ala	' CGG Arg	CTG Leu	CTG Leu 870	2610
			C GAG o Glu		Glu					Gly					
ATC Ile	C AAC	G TGC S Trp	G ATO	G GCG Ala 890	a Leu	GAG Glu	TCC Ser	ATT	CTC Leu 895	ı Arç	C CGG g Aro	G CGG g Arg	TTC Phe	ACC Thr	2700

FIG. 15. (CONTINUED)

CAC CAG AGT GAT GTG TGG AGT TAT GGT GTG ACT GTG TGG GAG CTG 2745 His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr Val Trp Glu Leu 910 905 915 ATG ACT TTT GGG GCC AAA CCT TAC GAT GGG ATC CCA GCC CGG GAG 2790 Met Thr Phe Gly Ala Lys Pro Tyr Asp Gly Ile Pro Ala Arg Glu 925 920 930 ATC CCT GAC CTG CTG GAA AAG GGG GAG CGG CTG CCC CAG CCC CCC 2835 Ile Pro Asp Leu Leu Glu Lys Lgy Glu Arg Leu Pro Gln Pro Pro 935 ATC TGC ACC ATT GAT GTC TAC ATG ATC ATG GTC AAA TGT TGG ATG 2880 Ile Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp Met 950 955 960 ATT GAC TCT GAA TGT CGG CCA AGA TTC CGG GAG TTG GTG TCT GAA 2925 Ile Asp Ser Glu Cys Arg Pro Arg Phe Arg Glu Leu Val Ser Glu 970 TTC TCC CGC ATG GCC AGG GAC CCC CAG CGC TTT GTG GTC ATC CAG 2970 Phe Ser Arg Met Ala Arg Asp Pro Gln Arg Phe Val Val Ile Gln 990 980 985 AAT GAG GAC TTG GGC CCA GCC AGT CCC TTG GAC AGC ACC TTC TAC 3015 Asn Glu Asp Leu Gly Pro Ala Ser Pro Leu Asp Ser Thr Phe Tyr 995 1000 1005 CGC TCA CTG CTG GAG GAC GAT GAC ATG GGG GAC CTG GTG GAT GCT 3060 Arq Ser Leu Leu Glu Asp Asp Met Gly Asp Leu Val Asp Ala 1015 1010 GAG GAG TAT CTG GTA CCC CAG CAG GGC TTC TTC TGT CCA GAC CCT 3105 Glu Glu Tyr Leu Val Pro Gln Gln Gly Phe Phe Cys Pro Asp Pro 1035 1030 1025 GCC CCG GGC GCT GGG GGC ATG GTC CAC CAC AGG CAC CGC AGC TCA 3150 Ala Pro Gly Ala Gly Gly Met Val His His Arg His Arg Ser Ser 1045 1050 1040 TCT ACC AGG AGT GGC GGT GGG GAC CTG ACA CTA GGG CTG GAG CCC 3195 Ser Thr Arg Ser Gly Gly Gly Asp Leu Thr Leu Gly Leu Glu Pro 1055 1060 1065 TCT GAA GAG GAC CCC AGG TCT CCA CTG GCA CCC TCC GAA GGG 3240 Ser Glu Glu Glu Ala Pro Arg Ser Pro Leu Ala Pro Ser Glu Gly 1075 1080 1070

FIG. 15. (CONTINUED)

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GCT GGC TCC GAT GTA TTT GAT GGT GAC CTG GGA ATG GGG GCA GCC 3285 Ala Gly Ser Asp Val Phe Asp Gly Asp Leu Gly Met Gly Ala Ala 1085 1090 AAG GGG CTG CAA AGC CTC CCC ACA CAT GAC CCC AGC CCT CTA CAG 3330 Lys Gly Leu Gln Ser Leu Pro Thr His Asp Pro Ser Pro Leu Gln 1100 1105 1110 CGG TAC AGT GAG GAC CCC ACA GTA CCC CTG CCC TCT GAG ACT GAT 3375 Arg Tyr Ser Glu Asp Pro Thr Val Pro Leu Pro Ser Glu Thr Asp 1115 1125 1120 GGC TAC GTT GCC CCC CTG ACC TGC AGC CCC CAG CCT GAA TAT GTG 3420 Gly Tyr Val Ala Pro Leu Thr Cys Ser Pro Gln Pro Glu Tyr Val 1135 1140 1130 AAC CAG CCA GAT GTT CGG CCC CAG CCC CCT TCG CCC CGA GAG GGC 3465 Asn Gln Pro Asp Val Arg Pro Gln Pro Pro Ser Pro Arg Glu Gly 1145 1150 CCT CTG CCT GCT GCC CGA CCT GCT GGT GCC ACT CTG GAA AGG CCC 3510 Pro Leu Pro Ala Ala Arg Pro Ala Gly Ala Thr Leu Glu Arg Pro 1160 1165 AAG ACT CTC TCC CCA GGG AAG AAT GGG GTC GTC AAA GAC GTT TTT 3555 Lys Thr Leu Ser Pro Gly Lys Asn Gly Val Val Lys Asp Val Phe 1175 1180 1185 GCC TTT GGG GGT GCC GTG GAG AAC CCC GAG TAC TTG ACA CCC CAG 3600 Ala Phe Gly Gly Ala Val Glu Asn Pro Glu Tyr Leu Thr Pro Gln 1195 1200 1190 GGA GGA GCT GCC CCT CAG CCC CAC CCT CCT GCC TTC AGC CCA 3645 Gly Gly Ala Ala Pro Gln Pro His Pro Pro Pro Ala Phe Ser Pro 1210 1215 1205 GCC TTC GAC AAC CTC TAT TAC TGG GAC CAG GAC CCA CCA GAG CGG 3690 Ala Phe Asp Asn Leu Tyr Tyr Trp Asp Gln Asp Pro Pro Glu Arg 1220 1225 GGG GCT CCA CCC AGC ACC TTC AAA GGG ACA CCT ACG GCA GAG AAC 3735 Gly Ala Pro Pro Ser Thr Phe Lys Gly Thr Pro Thr Ala Glu Asn 1240 1245 1235 3768 CCA GAG TAC CTG GGT CTG GAC GTG CCA GTG TGA Pro Glu Tyr Leu Gly Leu Asp Val Pro Val 1250

FIG. 15. (CONTINUED)

ccgggccgga gccgcaatga tcatcatgga gctggcggcc tggtgccgct 50 gggggtteet eetegeeete etgeeeeeg gaategeggg cacceaagtg 100 tgtaccggca cagacatgaa gttgcggctc cctgccagtc ctgagaccca 150 cctggacatg ctccgccacc tgtaccaggg ctgtcaggta gtgcagggca 200 acttggagct tacctacgtg cctgccaatg ccagcctctc attcctgcag 250 gacatccagg aagttcaggg ttacatgctc atcgctcaca accaggtgaa 300 gcgcgtccca ctgcaaaggc tgcgcatcgt gagagggacc cagctctttg 350 aggacaagta tgeeetgget gtgetagaca acegagatee teaggacaat 400 gtcgccgcct ccaccccagg cagaacccca gaggggctgc gggagctgca 450 gcttcgaagt ctcacagaga tcctgaaggg aggagttttg atccgtggga 500 acceteaget etgetaceag gacatggttt tgtggaagga egtetteege 550 aagaataacc aactggctcc tgtcgatata gacaccaatc gttcccgggc 600 ctgtccacct tgtgcccccg cctgcaaaga caatcactgt tggggtgaga 650 gtccggaaga ctgtcagatc ttgactggca ccatctgtac cagtggttgt 700 gcccggtgca agggccggct gcccactgac tgctgccatg agcagtgtgc 750 cqcaqqctqc acqgqcccca agcattctga ctgcctggcc tgcctccact 800 tcaatcatag tggtatctgt gagctgcact gcccagccct cgtcacctac 850 aacacagaca cctttgagtc catgcacaac cctgagggtc gctacacctt 900 tggtgccagc tgcgtgacca cctgccccta caactacctg tctacggaag 950 tgggatcctg cactctggtg tgtcccccga ataaccaaga ggtcacagct 1000 gaggacggaa cacagcgttg tgagaaatgc agcaagccct gtgctcgagt 1050 gtgctatggt ctgggcatgg agcaccttcg aggggcgagg gccatcacca 1100 gtgacaatgt ccaggagttt gatggctgca agaagatctt tgggagcctg 1150 gcatttttgc cggagagctt tgatggggac ccctcctccg gcattgctcc 1200 gctgaggcct gagcagctcc aagtgttcga aaccctggag gagatcacag 1250 gttacctgta catctcagca tggccagaca gtctccgtga cctcagtgtc 1300 ttccagaacc ttcgaatcat tcggggacgg attctccacg atggcgcgta 1350 ctcattgaca ctgcaaggcc tggggatcca ctcgctgggg ctgcgctcac 1400 tgcgggagct gggcagtgga ttggctctga ttcaccgcaa cgcccatctc 1450 tgctttgtac acactgtacc ttgggaccag ctcttccgga acccacatca 1500 ggccctgctc cacagtggga accggccgga agaggacttg tgcgtctcga 1550 gcggcttggt ctgtaactca ctgtgtgccc acgggcactg ctgggggcca 1600 gggcccaccc agtgtgtcaa ctgcagtcat ttccttcggg gccaggagtg 1650 tgtggaggag tgccgagtat ggaaggggct cccccgggag tatgtgagtg 1700 acaagcgctg tctgccgtgt caccccgagt gtcagcctca aaacagctca 1750 gagacctgct ttggatcgga ggctgatcag tgtgcagcct gcgcccacta 1800 caaggactcg tcctcctgtg tggctcgctg ccccagtggt gtgaaaccgg 1850 acctctccta catgcccatc tggaagtacc cggatgagga gggcatatgc 1900 cagccgtgcc ccatcaactg cacccactcc tgtgtggatc tggatgaacg 1950 aggctgccca gcagagcaga gagccagccc ggtgacattc atcattgcaa 2000 ctgtagaggg cgtcctgctg ttcctgatct tagtggtggt cgttggaatc 2050 ctaatcaaac gaaggagaca gaagatccgg aagtatacga tgcgtaggct 2100 gctgcaggaa actgagttag tggagccgct gacgcccagc ggagcaatgc 2150 ccaaccaggc tcagatgcgg atcctaaaag agacggagct aaggaaggtg 2200 aaggtgcttg gatcaggagc ttttggcact gtctacaagg gcatctggat 2250 cccagatggg gagaatgtga aaatccccgt ggctatcaag gtgttgagag 2300 aaaacacatc tcctaaagcc aacaaagaaa ttctagatga agcgtatgtg 2350

FIG. 16. (SEQ ID NO: 10)

	+~~~++~+	~+ ~+ ~+ ~+ ~	agaat aat aa	aaatataaat	2400
atggctggtg		gtatgtgtcc		gcatctgcct	2450
gacatccaca	gtacagctgg	tgacacagct	tatgccctac	ggctgccttc	2500
tggaccatgt	ccgagaacac	cgaggtcgcc	taggctccca	ggacctgctc	2550
aactggtgtg	ttcagattgc	caaggggatg	agctacctgg	aggacgtgcg	
gcttgtacac	agggacctgg	ctgcccggaa	tgtgctagtc	aagagtccca	2600
accacgtcaa	gattacagat	ttcgggctgg	ctcggctgct	ggacattgat	2650
gagacagagt	accatgcaga	tgggggcaag	gtgcccatca	aatggatggc	2700
attggaatct	attctcagac	gccggttcac	ccatcagagt	gatgtgtgga	2750
gctatggagt	gactgtgtgg	gagctgatga	cttttggggc	caaaccttac	2800
gatggaatcc	cagcccggga	gatccctgat	ttgctggaga	agggagaacg	2850
cctacctcag	cctccaatct	gcaccattga	tgtctacatg	attatggtca	2900
aatgttggat	gattgactct	gaatgtcgcc	cgagattccg	ggagttggtg	2950
tcagaatttt	cacgtatggc	gagggacccc	cagcgttttg	tggtcatcca	3000
gaacgaggac	ttgggcccat	ccagccccat	ggacagtacc	ttctaccgtt	3050
cactgctgga	agatgatgac	atgggtgacc	tggtagacgc	tgaagagtat	3100
ctggtgcccc	agcagggatt	cttctccccg	gaccctaccc	caggcactgg	3150
gagcacagcc	catagaaggc	accgcagctc	gtccaccagg	agtggaggtg	3200
gtgagctgac	actgggcctg	gagccctcgg	aagaagggcc	ccccagatct	3250
ccactggctc	cctcggaagg	ggctggctcc	gatgtgtttg	atggtgacct	3300
ggcaatgggg	gtaaccaaag	ggctgcagag	cctctctcca	catgacctca	3350
gccctctaca	gcggtacagc	gaggacccca	cattacctct	gccccccgag	3400
actgatggct	atgttgctcc	cctggcctgc	agcccccagc	ccgagtatgt	3450
gaaccaatca	gaggttcagc		tttaacccca	gagggtcctc	3500
tgcctcctgt	ccggcctgct	ggtgctactc	tagaaagacc	caagactctc	3550
tctcctggga	agaatggggt	tgtcaaagac	gtttttgcct	tcgggggtgc	3600
tgtggagaac	cctgaatact	tagtaccgag	agaaggcact	gcctctccgc	3650
cccacccttc	tcctgccttc	agcccagcct	ttgacaacct	ctattactgg	3700
gaccagaact	catcggagca		ccaagtaact	ttgaagggac	3750
ccccactgca	gagaaccctg	agtacctagg	cctggatgta	cctgtatgag	3800
acgtgtgcag	acgtcctgtg	ctttcagagt	ggggaaggcc	tgacttgtgg	3850
tctccatcgc	cacaaagcag			attacatcca	3900
gggcagacgg	ctctaccagg		gaggaacctt	tccttgctgc	3850
ttgaa	3955			. , -, -, -	
5					

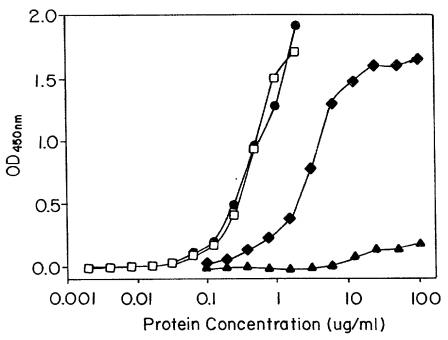
FIG. 16. (CONTINUED)

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Control of white wife the street will be control to the control to the state of the

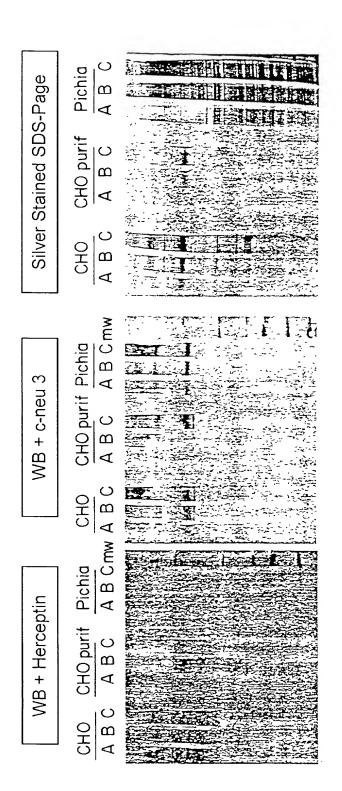
Herceptin Binding by Direct Elisa 10/5/99



- ECD-PD (mammalian derived)
- -- ECD-PD (mammalian derived)
- hECD-PD-CHis (E. coli derived and refolded, with C-HisTag)
- ◆ hECD-PD (E. coli derived and refolded, with N-HisTag)

FIG. 17.

Comparison of Her2neu ECD-PD Expression in CHO-K1 (S/SF) and Pichia (Non reducing conditions)



Legend: CHO; A, B, C = 2,5μl/ 5μl/ 10μl CHO purif; A, B, C = 125ng/ 250ng/ 500ng Pichia; A, B, C = 2,5μl/ 5μl/ 10μl from a 1/30 dilution of OD 120

16. 18.

			• •		
atggagctgg	cggcctggtg	ccgttggggg	ttcctcctcg	ccctcctgtc	50
ccccggagcc	gcgggtaccc	aagtgtgtac	cggtaccgac	atgaagttgc	100
gactccctgc	cagtcctgag	acccacctgg	acatgcttcg	ccacctctac	150
cagggctgtc	aggtggtgca	gggcaatttg		acctgcccgc	200
caatgccagc	ctctcattcc	tgcaggacat	ccaggaagtc	cagggataca	250
tgctcatcgc	tcacaaccga	gtgaaacacg	tcccactgca	gaggttgcgc	300
atcgtgagag	ggactcagct	ctttgaggac	aagtatgccc	tggctgtgct	350
agacaaccga	gaccctttgg	acaacgtcac	caccgccgcc	ccaggcagaa	400
ccccagaagg	gctgcgggag	ctgcagcttc	gaagtctcac	agagatcttg	450
aagggaggag	ttttgatccg	tgggaaccct	cagctctgct	accaggacat	500
ggttttgtgg	aaggatgtcc	tccgtaagaa	taaccagctg	gctcctgtcg	550
acatggacac	caatcgttcc	cgggcctgtc	caccttgtgc	cccaacctgc	600
aaagacaatc	actgttgggg	tgagagtcct	gaagactgtc	agatcttgac	650
tggcaccatc	tgtactagtg	gctgtgcccg	gtgcaagggc	cggctgccca	700
ctgactgttg	ccatgagcag	tgtgctgcag	gctgcacggg	tcccaagcat	750
tctgactgcc	tggcctgcct	ccacttcaat	catagtggta	tctgtgagct	800
gcactgcccg	gccctcatca	cctacaacac	agacaccttc	gagtccatgc	850
tcaaccctga	gggtcgctac	acctttggtg	ccagctgtgt	gaccacctgc	900
ccctacaact	acctctccac	ggaagtggga	tcctgcactc	tggtctgtcc	950
cccgaacaac	caagaggtca	cagctgagga	cggaacacag	cggtgtgaga	1000
aatgcagcaa	gccctgtgct	ggagtatgct	atggtctggg	catggagcac	1050
ctccgagggg	cgagggccat	caccagtgac	aatatccagg	agtttgctgg	1100
ctgcaagaag	atctttggga	gcctggcatt	tttgccggag	agctttgatg	1150
ggaacccctc	ctccggcgtt	gccccactga	agccagagca	tctccaagtg	1200
ttcgaaaccc	tggaggagat	cacaggttac	ctatacattt	cagcatggcc	1250
agagagcttc	caagacctca	gtgtcttcca	gaaccttcgg	gtcattcggg	1300
gacggattct	ccatgatggt	gcttactcat	tgacgttgca	aggcctgggg	1350
attcactcac	tggggctacg	ctcactgcgg	gagctgggca	gtggattggc	1400
tctcattcac	cgcaacaccc	atctctgctt	tgtaaacact	gtaccttggg	1450
accagctctt	ccggaacccg	caccaggccc	tactccacag	tgggaaccgg	1500
ccagaagagg	catgtggtct	tgagggcttg	gtctgtaact	cactgtgtgc	1550
ccgtgggcac	tgctgggggc	cagggcccac	ccagtgtgtc	aactgcagtc	1600
agttcctccg	gggccaggag	tgtgtggagg	agtgccgagt	atggaagggg	1650
ctccccaggg	agtatgtgag	gggcaagcac	tgtctgccat	gccaccccga	1700
gtgtcagcct	caaaacagct	cggagacctg	ctatggatcg	gaggctgacc	1750
agtgtgaggc	ttgtgcccac	tacaaggact	catcttcctg	tgtggctcgc	1800
				tctggaagta	1850
cccggatgag				tgcacccact	1900
catgtgtgga				gagagccagc	1950
ccagtgacat		aactgtggtg	ggcgtcctgt	tgttcctgat	2000
catagtggtg	gtcattggaa			cagaagatcc	2050
ggaagtatac	catgcgtagg			ggtggagccg	2100
ctgacgccca	gtggagctgt			ggatcctaaa	2150
ggagacagag				gccttcggca	2200
	gggcatctgg			gaaaatcccc	2250
gtggccatca			tctcctaaag	ctaacaaaga	
aatcctagat		tcatggctgg	tgtgggttct	ccatatgtgt	2350

FIG. 19. (SEQ ID NO: 11)

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Company and American Phillips and Company

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cccgcctcct gggcatctgc ctgacatcca cagtgcagct ggtgacaca	q 2400
cttatgccct atggctgcct tctggaccat gtccgagaac accgaggtc	0 4 5 0
cttaggctcc caggacctgc tcaactggtg tgttcagatt gccaagggg	
tgagctacct ggaggaagtt cggcttgttc acagggacct agctgcccg	
aacgtgctag tcaagagtcc caaccacgtc aagattaccg acttcgggc	
ggcacggctg ctggacattg atgagactga ataccatgca gatgggggc	
aggtgcccat caagtggatg gcattggaat ctattctcag acgccggtt	
actcatcaga gtgatgtgtg gagctatggt gtgactgtgt gggagctga	
gacctttggg gccaaacctt acgatgggat cccagctcgg gagatccct	
atttgctgga gaagggagaa cgcctacctc agcctccaat ctgcaccat	_
gacgtctaca tgatcatggt caaatgttgg atgattgact ccgaatgtc	
cccqaqattc cgggagttgg tatcagaatt ctcccgtatg gcaagggac	_
cccaqcqctt tqtqqtcatc cagaacgagg acttaggccc ctccagccc	
atggacagca cettetaceg tteactgetg gaggatgatg acatggggg	
gctggtcgat gctgaagagt acctggtacc ccagcaggga ttcttctcc	
cagaccetge cetaggtact gggagcacag cecacegeag acacegeag	
tcgtcggcca ggagtggcgg tggtgagctg acactgggcc tggagccct	
ggaagaagag cccccagat ctccactggc tccctccgaa ggggctggc	
ccgatgtgtt tgatggtgac ctggcagtgg gggtaaccaa aggactgca	
agcctctctc cacatgacct cagccctcta cagcggtaca gtgaggato	
cacattacct ctgcccccg agactgatgg ctacgttgct cccctggcc	
gcagcccca gcccgagtat gtgaaccagc cagaggttcg gcctcagto	
cccttgaccc cagagggtcc tccgcctccc atccgacctg ctggtgcta	
totagaaaga cocaagacto tototootgg gaaaaatggg gttgtcaaa	00
acgtttttgc ctttgggggt gctgtggaga accctgaata cctagcacc	
agagcaggca ctgcctctca gccccaccct tctcctgcct tcagccca	
ctttgacaac ctctattact gggaccagaa ctcatcggag cagggtcc	0 - 0 0
caccaagtac ctttgaaggg accccactg cagagaaccc tgagtacc	
ggcctggatg tgccagtatg a	3771

FIG. 19.(CONTINUED)

Met Glu Leu Ala Ala Trp Cys Arg Trp Gly Phe Leu Leu Ala Leu Leu Ser Pro Gly Ala Ala Gly Thr Gln Val Cys Thr Gly Thr Asp Met Lys Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr Leu Pro Ala Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val Gln Gly Tyr Met Leu Ile Ala His Asn Arg Val Lys His Val Pro Leu Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Lys Tyr Ala Leu Ala Val Leu Asp Asn Arg Asp Pro Leu Asp Asn Val Thr Thr Ala Ala Pro Gly Arg Thr Pro Glu Gly Leu Arg Glu Leu Gln Leu Arg Ser Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Arg Gly Asn Pro Gln Leu Cys Tyr Gln Asp Met Val Leu Trp Lys Asp Val Leu Arg Lys Asn Asn Gln Leu Ala Pro Val Asp Met Asp Thr Asn Arg Ser Arg Ala Cys Pro Pro Cys Ala Pro Thr Cys Lys Asp Asn His Cys Trp Gly Glu Ser Pro Glu Asp Cys Gln Ile Leu Thr Gly Thr Ile Cys Thr Ser Gly Cys Ala Arg Cys Lys Gly Arg Leu Pro Thr Asp Cys Cys His Glu Gln Cys Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys

FIG. 20. (SEQ ID NO: 14)

Leu His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Ile Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Leu Asn Pro Glu Gly Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Thr Cys Pro Tyr Asn Tyr Leu Ser Thr Glu Val Gly Ser Cys Thr Leu Val Cys Pro Pro Asn Asn Gln Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys Pro Cys Ala Gly Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Gly Ala Arg Ala Ile Thr Ser Asp Asn Ile Gln Glu Phe Ala Gly Cys Lys Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asn Pro Ser Ser Gly Val Ala Pro Leu Lys Pro Glu His Leu Gln Val Phe Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro Glu Ser Phe Gln Asp Leu Ser Val Phe Gln Asn Leu Arg Val Ile Arg Gly Arg Ile Leu His Asp Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu Gly Ile His Ser Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly Leu Ala Leu Ile His Arg Asn Thr His Leu Cys Phe Val Asn Thr Val Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Ser Gly Asn Arg Pro Glu Glu Ala Cys Gly Leu Glu Gly Leu Val Cys

Asn Ser Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys Arg Val Trp Lys Gly Leu Pro Arg Glu Tyr Val Arg Gly Lys His Cys Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Ser Ser Glu Thr Cys Tyr Gly Ser Glu Ala Asp Gln Cys Glu Ala Cys Ala His Tyr Lys Asp Ser Ser Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu Ser Tyr Met Pro Ile Trp Lys Tyr Pro Asp Glu Glu Gly Ile Cys Gln Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Glu Arg Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Val Thr Phe Ile Ile Ala Thr Val Val Gly Val Leu Leu Phe Leu Ile Ile Val Val Val Ile Gly Ile Leu Ile Lys Arg Arg Gln Lys Ile Arg Lys Tyr Thr Met Arg Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser Gly Ala Val Pro Asn Gln Ala Gln Met Arg Ile Leu Lys Glu Thr Glu Leu Arg Lys Leu Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr Lys Gly Ile Trp Ile Pro Asp Gly Glu Asn Val Lys Ile Pro Val Ala Ile Lys Val Leu Arg Glu Asn Thr Ser Pro Lys Ala Asn Lys Glu Ile

Leu Asp Glu Ala Tyr Val Met Ala Gly Val Gly Ser Pro Tyr Val Ser Arg Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Val Thr Gln Leu Met Pro Tyr Gly Cys Leu Leu Asp His Val Arg Glu His Arg Gly Arg Leu Gly Ser Gln Asp Leu Leu Asn Trp Cys Val Gln Ile Ala Lys Gly Met Ser Tyr Leu Glu Glu Val Arg Leu Val His Arg Asp Leu Ala Ala Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys Ile Thr Asp Phe Gly Leu Ala Arg Leu Leu Asp Ile Asp Glu Thr Glu Tyr His Ala Asp Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu Arg Arg Arg Phe Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr Val Trp Glu Leu Met Thr Phe Gly Ala Lys Pro Tyr Asp Gly Ile Pro Ala Arq Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln Pro Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp Met Ile Asp Ser Glu Cys Arg Pro Arg Phe Arg Glu Leu Val Ser Glu Phe Ser Arg Met Ala Arg Asp Pro Gln Arg Phe Val Val Ile Gln Asn Glu Asp Leu Gly Pro Ser Ser Pro Met Asp Ser Thr Phe Tyr Arg Ser Leu Leu Glu Asp Asp Met Gly Glu Leu Val Asp Ala Glu Glu Tyr

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Leu 1025		Pro	Gln		Gly .030	Phe	Phe	Ser		Asp .035	Pro	Ala	Leu	Gly 1	Thr 040
Gly	Ser	Thr		His .045	Arg	Arg	His		Ser .050	Ser	Ser	Ala		Ser 1055	Gly
Gly	Gly		Leu .060	Thr	Leu	Gly		Glu .065	Pro	Ser	Glu		Glu 1070	Pro	Pro
Arg		Pro .075	Leu	Ala	Pro		Glu .080	Gly	Ala	Gly		Asp L085	Val	Phe	Asp
-	Asp .090	Leu	Ala	Val	_	Val .095	Thr	Lys	Gly		Gln L100	Ser	Leu	Ser	Pro
His 1105		Leu	Ser		Leu L110	Gln	Arg	Tyr		Glu 1115	Asp	Pro	Thr	Leu 1	Pro 120
Leu	Pro	Pro		Thr L125	Asp	Gly	Tyr		Ala 1130	Pro	Leu	Ala		Ser 1135	Pro
Gln	Pro		Tyr 1140	Val	Asn	Gln		Glu 1145	Val	Arg	Pro		Ser 1150	Pro	Leu
Thr		Glu 1155	Gly	Pro	Pro		Pro 1160	Ile	Arg	Pro		Gly 1165	Ala	Thr	Leu
	Arg L170	Pro	Lys	Thr		Ser 1175	Pro	Gly	Lys		Gly 1180	Val	Val	Lys	Asp
Val 1185		Ala	Phe		Gly 1190	Ala	Val	Glu		Pro 1195	Glu	Tyr	Leu	Ala	Pro 1200
Arg									Pro 1210					Ser 1215	Pro
Ala	Phe		Asn 1220	Leu	Tyr	Tyr		Asp 1225	Gln	Asn	Ser		Glu 1230	Gln	Gly
Pro		Pro 1235		Thr	Phe		Gly 1240	Thr	Pro	Thr		Glu 1245		Pro	Glu
_	Leu 1250	Gly	Leu	Asp		Pro 1255									